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Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

VIA COURIER

Amendment to Citizen Petition
Docket Number 02P-0414/CP1
Inclusion of Pediatric Waiver Request

Dear Sir or Madam:

The petition cited above was submitted on September 13, 2002. The petition requested the Commissioner of the Food and Drug Administration to declare that the drug product **Cefuroxime Axetil Tablets for Oral Suspension 125 mg and 250 mg** is suitable for submission as an Abbreviated New Drug Application (ANDA).

In December of 2003, Congress passed the Pediatric Research Equity Act (PREA) of 2003 that amended the Federal Food, Drug and Cosmetic Act (The Act) to provide the Agency authority to require drug firms to study certain drugs in pediatric patients, if the Agency felt that such study would provide beneficial health data for that patient population. This letter is based on the requirements outlined in PREA and references the Draft Guidance for Industry [Recommendations for Complying with the Pediatric Rule (21 CFR 314.55(a) and 601.27(a)), dated November 2000].

Reference is also made to the Agency's communication dated February 3, 2004, recommending submission of a waiver with supporting information and documentation in accordance with the provisions of Section 2 of PREA as an amendment to the suitability petition.

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AMD 1

Section 505B(a)(4)(A)(iii) of The Act (as amended by PREA) provides a provision for a waiver from such requirement if:

> (iii) the drug or biological product --
>
> > (I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and
> >
> > (II) is not likely to be used in a substantial number of pediatric patients.

The petitioner hereby requests that a waiver from the conduct of pediatric studies for all age groups be granted for this petition.

The Reference Listed Drug Ceftin® Powder for Oral Suspension (cefuroxime axetil 125 mg/5 mL and 250 mg/5 mL) (GlaxoSmithKline) is currently available in a powder for oral suspension and is, according to the approved labeling, indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of certain designated microorganisms in conditions such as pharyngitis/tonsillitis, otitis media and impetigo.

The petitioner's proposed product, Tablets for Oral Suspension, forms an oral suspension on dispersion similar to the Reference Listed Drug. This petition requests a change in dosage form from "Powder for Oral Suspension" to "Tablets for Oral Suspension." The final dosage form consumed by the patient is the "suspension" and is identical for both the petitioner's product and the Reference Listed Drug.

The proposed product, Cefuroxime Axetil Tablets for Oral Suspension (125 mg and 250 mg), is designed to provide patients a more convenient dosage form of cefuroxime axetil with respect to unit-dose dispensing, ease of administration to patients who have difficulty swallowing, and storage and administration (for example, during travel). These benefits, while not excluding pediatrics, are directed to the adult population. The petitioner believes that Cefuroxime Axetil Tablets for Oral Suspension does not represent a meaningful therapeutic benefit over existing antibiotic therapies or over the Reference Listed Drug, Ceftin® Powder for Oral Suspension, for the pediatric patient population.

Furthermore, the petitioner believes that additional clinical studies in the pediatric population with the petitioner's tablets for oral suspension would not offer meaningful data, nor would they demonstrate a therapeutic benefit over Ceftin® Powder for Oral Suspension in the pediatric population for which it is intended. As stated in the product labeling for Ceftin® Powder for Oral Suspension (125 mg/5 mL and 250 mg/5 mL), pediatric studies have been conducted and the product labeling contains adequate dosing and administration information for the pediatric population from ages 3 months to 12 years:

Children 3 months to 12 years: Dosage varies with infection type. For pharyngitis/ tonsillitis, 20 mg/kg/day divided in two doses. For other infections, 30 mg/kg/day divided in two doses.

The planned labeling for Cefuroxime Axetil Tablets for Oral Suspension will be very similar in providing dose information for the allowable weight groups:

Children 3 months to 12 years: Dosage varies with infection type. For pharyngitis/ tonsillitis, administer 20 mg/kg/day divided in two doses. For example, for a child of approximately 13 kg, suspend and have the child drink one-125 mg tablet in water every 12 hours. For other infections, administer 30 mg/kg/day divided in two doses. For example, for a child of approximately 8 kg, suspend and have the child drink one-125 mg tablet in water every 12 hours (see Table 1 below). The child must drink the entire volume of suspended drug.

TABLE 1.
NUMBER OF CEFUROXIME AXETIL TABLETS FOR ORAL SUSPENSION TO BE GIVEN TO ACHIEVE RECOMMENDED DOSES

RECOMMENDED DOSAGE OF CEFUROXIME AXETIL TABLETS FOR ORAL SUSPENSION	CHILD'S WEIGHT (KG)	NUMBER OF TABLETS FOR SUSPENSION PER DOSE
10 mg/kg, every 12 hours (20 mg/kg/day)	13	One-125 mg tablet
	25	One-250 mg tablet
15 mg/kg, every 12 hours (30 mg/kg/day)	8	One-125 mg tablet
	17	One-250 mg tablet

Further, a bioequivalence study is planned comparing the Reference Listed Drug with Cefuroxime Axetil Tablets for Oral Suspension, and a product demonstrated to be bioequivalent in adults is accepted to be bioequivalent in a pediatric population. Therefore, additional studies would be redundant and unnecessary.

The planned bioequivalence study will compare Ceftin® Powder for Oral Suspension (250 mg/5 mL) with Cefuroxime Axetil Tablets for Oral Suspension (250 mg) in adult volunteers. The petitioner believes that the bioequivalence study conducted on adults should be adequate to demonstrate bioequivalence in children.

According to the approved labeling, Ceftin® Powder for Oral Suspension is recommended for use in pediatric patients 3 months to 12 years of age. The petitioner's product, in line with Ceftin®, is also indicated for use in pediatric patients 3 months to 12 years of age within the correct weight range for dosing. Based on the limited pediatric patient population in the appropriate weight ranges that can be dosed, the petitioner believes that there will not be

substantial use of the product in pediatric patients, and therefore a pediatric study is not warranted.

For the reasons stated above and consistent with the provisions of the Pediatric Research Equity Act of 2003, the petitioner respectfully requests that this waiver be granted.

Sincerely,

Nicholas M. Fleischer, R.Ph., Ph.D.
Director of Biopharmaceutics
THE WEINBERG GROUP INC.

NMF/kh

cc Gary Buehler, Director, Office of Generic Drugs